Case reports

Rhabdomyolysis Due to Diuretic Treatment

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A case of rhabdomyolysis due to hypokalemia after diuretic treatment is described in our study. Reviewing the relevant international literature we found that although the specific electrolytic disorder is responsible for 14% - 28% of the total cases of rhabdomyolysis, quite often it remains undiagnosed. The interesting point in our case is that patient's symptoms, electrocardiographic changes and abnormal enzymes values could possibly disorientate our diagnostic thought towards an acute coronary syndrome. Nevertheless, careful and detailed evaluation of patient's history, clinical manifestations and laboratory examinations, set the strong suspicion of rhabdomyolysis, that was confirmed by the elevated values of myoglobulin in serum and urine. After proper medical treatment the patient recovered promptly with a complete restoration of her clinical and laboratory profile.

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Diuretics probably consist the most widely and longitudinally used group of drugs for the treatment of cardiovascular disease. One of their most frequent side-effects is hypokalemia, which is found in about 35%-50% of patients receiving thiazide or loop diuretics. This hypokalemia is usually mild and when the patient is under proper medical supervision, it is easily recognized and treated. Nevertheless, in cases of patients who neglect to visit their doctor, it is possible that the diuretic induced hypokalemia could become extremely severe and even life-threatening. A frequently undiagnosed serious complication of hypokalemia is rhabdomyolysis.

We present a case of rhabdomyolysis provoked by diuretic induced hypokalemia. Careful approach and detailed evaluation of our patient's history, clinical manifestations and laboratory findings, set the strong suspicion of rhabdomyolysis, that was confirmed by the elevated values of myoglobulin in serum and urine.

Case report

A 72 year old woman was admitted to our hospital because of weakness, fatigue and diffused muscular pain located in the thorax and the upper extremities, in combination with abnormal ECG (bigeminy, ST-T segment changes) and abnormal enzyme values.

The present illness, had begun 10 days before with fatigue and weakness, while in the previous 48 hours palpitations and diffused muscular pain in the thoracic area, back and upper extremities, were added to the patients symptoms. Three days before the beginning of her symptoms, our patient mentioned vigorous physical activity.

Personal medical history included systemic arterial hypertension on treatment with thiazide diuretic and dyslipidaemia.

On clinical examination the patient was pale, with an arterial blood pressure of 120/70 mmHg, and a heart rate of 70 bpm. Heart auscultation revealed arrhythmia and normal heart sounds without

any audible cardiac murmurs or pericardial friction. Lung auscultation revealed a mild hoarseness of breath.

ECG revealed sinus rhythm with intermittent periods of bigeminy, ST segment depression up to 1,5 mm in V3, V4 and V5 leads, ST segment elevation up to 1 mm in aVR, T wave amplitude depression and a U wave in I, aVR , aVL and V5 leads.

The chest x-ray and complete blood count (CBC) were normal while erythrocyte sedimentation rate was slightly increased (ESR=58 mm/h). Biochemical control revealed an extremely increased value of creatine phosphokinase (CPK=13.025 IU/L), while the value of CPK-MB was only 223 IU/L (1,7% of total CPK). SGOT, SGPT and LDH were also considerably increased (SGOT=247 IU/L, SGPT=118 IU/L and LDH=614 IU/L). Another impressive finding was the very low potassium and chloride concentration in serum (K^+=1.8 mEq/L, CL^-=89 mEq/L), while the remaining electrolyte values were within normal limits. Blood gasses were typical of hypokalemic metabolic alkalosis (pH=7,6, PO_2=60 mmHg, PCO_2=45 mmHg, HCO_3=46.7 mmol/L, base excess =+22.3 mmol/L). Finally, apart from the slightly increased values of uric acid (UA =7.2 mg/dl) and total cholesterol (TCHOL=227 mg/dl), the remaining biochemical report was normal. Troponin T test was negative. Tests for viruses CMV, EBV, HBV, HCV, HIV, HSV 1&2 and tests for antibodies such as ANA, AMA, ASMA, anti-DNA and Ra-test, were negative.

The echocardiographic study was normal with the exception of a slightly dilated left atrium (4.2cm) and Doppler findings of left ventricle diastolic dysfunction.

Patient history of intense physical activity in association with the symptoms, the findings from clinical examination, the ECG changes (which were not typical of an acute coronary syndrome but were absolutely compatible with the established severe hypokalemia), the normal echocardiogram and the extremely increased enzyme values, (suggestive of muscular damage, along with the fact that serum concentrations of CK-MB and Troponin T were within normal limits), set the strong suspicion of rhabdomyolysis from the beginning. For this reason we proceeded with evaluation of serum and urine concentrations of myoglobulin. The results confirmed the diagnosis of rhabdomyolysis. More specifically, myoglobulin values in serum were 174 μgr/L (normal limits 0-70 μgr/L) and in urine were 66 ngr/L (normal limits <20 ngr/L).

Medical treatment based on aggressive i.v. hydration, with saline enriched with potassium, at an infusion rate of 20 mEq of potassium/hour was initiated. Bicarbonates to alkalinize urine and avoid the possibility of kidney damage due to myoglobinuria were also administered. The patient promptly recovered with a complete restoration of her clinical and laboratory profile. Arrhythmia and patient's symptoms disappeared during the first 24 hours. From the 3rd day of treatment potassium supplementation was administered only per os and serum concentrations returned to normal on the 6th day. Blood pressure control was achieved with the combination of an angiotensin II antagonist and a calcium channel blocker. Ten days later, the patient was discharged in excellent condition.

Discussion

Diuretic therapy constitutes one of the most frequent causes of hypokalemia in clinical practice[1]. Factors aggravating the frequency and severity of the specific electrolytic disorder are: the decreased intake of potassium with food, a diet rich in salt, metabolic alkalosis and the simultaneous use of diuretics acting on different sections of nephron[2].

On the other hand, it is well known that a potassium deficit could cause important major or minor complications. These important complications include arrhythmias, muscular weakness and paralysis, glucose intolerance and rhabdomyolysis[3,4]. The severity of neuromuscular disorders tends to be proportionate to the rate at which hypokalemia develops. Diuretic induced hypokalemia proves to be one of the most frequent causes of rhabdomyolysis[5-12]. The specific electrolytic disorder is responsible for 14%-28% from the total cases of rhabdomyolysis[11,13]. Although the above mentioned percentage may seem overestimated, we must not forget that hypokalemia as a cause of rhabdomyolysis in many cases remains unrecognized. Muscle destruction due to rhabdomyolysis causes the release of large amounts of potassium in the circulation. Consequently, when the clinical syndrome of rhabdomyolysis is fully developed, the calculated concentrations of potassium in serum are found to be within normal limits or even slightly increased[12]. The two major and most commonly used groups of diuretics which cause an elevated loss of potassium in urine (i.e. loop diure-

tics and thiazides) are capable of causing, with similar frequency, rhabdomyolysis. On the other hand it is not a rare phenomenon, for some patients with rhabdomyolysis to present with acute renal failure because of a severe accompanying myoglobinuria[10,16].

We can distinguish three major groups of patients with rhabdomyolysis: a) patients with pure exertional rhabdomyolysis, b) patients with genetically transmitted defects in ATP generation and c) patients with one or more precipitating factors leading to rhabdomyolysis. Such factors are: alcoholism, potassium deficiency, phosphate deficiency, bacterial or virus infections, drugs or toxins (e.g. statins, cocaine, amphetamines, neuroleptics, tetanus toxin, snake venom toxin), direct injuries (e.g. crush, electric shock, burns), ischemic injuries (compression, sickle cell disease) and situations with long-standing muscular contraction or rigor (e.g. status epilepticus, malignant hyperthermia, malignant neuroleptic syndrome)[14-17].

The most frequent symptoms of rhabdomyolysis are fatigue, weakness, muscular pain and swelling, although, it is possible for some patients to be completely asymptomatic. The most usual complications are metabolic disturbances and acute renal failure. Diagnosis is based on history and laboratory findings typical for muscular damage. While in the past rhabdomyolysis was considered to be a relatively rare clinical entity, nowadays its diagnosis is set with increasing frequency, due to the convenience in the determination of basic laboratory examinations for the detection of muscular damage (i.e. CPK and myoglobulin) and due to the improved sensitivity for its presence in clinical situations predisposing to muscle destruction. Although, a specific CPK cut-off limit, has not been defined, above which the diagnosis of rhabdomyolysis is considered to be certain, concentrations of CPK in serum >10.000 IU/L are almost always indicative of severe rhabdomyolysis. Even in cases of extremely intense physical activity, CPK rarely exceeds >1000 IU/L[1]. If the patient has more than one episode of rhabdomyolysis, or there is a positive family history for the specific disorder, the clinical suspicion for an enzymatic defect should be heightened.

The form and duration of treatment should be individualized according to patient's condition[18]. In extremely severe cases hemodialysis is needed, in order to achieve restoration of electrolytic and acid-base balance.

In conclusion, in cases of patients who present with chest, shoulder and upper extremities pain, in combination with an abnormal ECG and increased serum concentrations of CPK, after the exclusion of an acute coronary syndrome, rhabdomyolysis should be at top of our diagnostic list, since the risk of this life threatening complication is considerably high[10,16].

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